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(12) **United States Patent**
Plachetka et al.(10) Patent No.: **US 6,479,551 B1**(45) Date of Patent: ***Nov. 12, 2002**(54) **TREATMENT OF MIGRAINE HEADACHE**(75) Inventors: **John R. Plachetka**, Chapel Hill, NC (US); **Zakauddin T. Chowhan**, Gaithersburg, MD (US)(73) Assignee: **Pozen Inc.**, Chapel Hill, NC (US)

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(56) **References Cited****U.S. PATENT DOCUMENTS**

2,099,402 A 11/1937 Keller 167/82
 4,024,279 A 5/1977 Zor et al. 514/56 T
 4,235,971 A 11/1980 Howard et al. 435/293
 4,380,540 A 4/1983 Poyser et al. 514/162
 4,999,226 A 3/1991 Schock et al. 424/472
 5,037,823 A 8/1991 Jones et al. 514/222.8
 5,055,306 A 10/1991 Barry et al. 424/482
 5,155,105 A 10/1992 Jones et al. 514/223.5
 5,437,874 A 8/1995 Bru et al. 424/466
 5,573,776 A 11/1996 Harrison et al. 424/435
 5,681,583 A 10/1997 Conte et al. 424/472
 5,885,616 A 3/1999 Hsiao et al. 424/472
 6,077,539 A * 6/2000 Plachetka et al. 424/474

FOREIGN PATENT DOCUMENTS

BE 881 967 6/1980
 CA 2020018 6/1990
 EP 774 253 5/1997
 WO WO 95/22947 8/1995

OTHER PUBLICATIONS

STN/CAS online, file EMBASE, Acc. No. 1999161935, (Mandell, Cleveland Clinic Journal of Medicine (1999), 66/5, pp. 285-292), Abstract.*

Dialog online, file Derwent WPI, EP774253, Abstract (1997). Albibi, "Metoclopramide: pharmacology and clinical application," *Annals of Internal Medicine*, (1983)98: 86-95.Anderson, "Double-blind study of naproxen vs placebo in the treatment of acute migraine attacks," *Cephalalgia* (1989) 9:29-32.Bateman, "Extrapyramidal reactions to metoclopramide and prochlorperazine" *Quarterly Journal of Medicine* (1989) 71(264):307-311.Baumel, "Migraine: A pharmacologic review with newer options and delivery modalities" *Neurology* (1994) 44 (Suppl 3) S13-S17.Becker "Pharmacokinetic aspects of a combination of metoclopramide and paracetamol. Results of a human kinetic study and consequences for migraine patients" *Arzneimittelforschung* (1992) 42(4):552-555 (including English language translation).Boureau "Comparison of subcutaneous sumatriptan with usual acute treatments for migraine. French sumatriptan study group." *Eur Neurol* (1995) 35(5):264-269.Capobianco "An overview of the diagnosis and pharmacologic treatment of migraine" *Mayo Clin Proc* (1996) 71:1055-1066.Chabriot "Combined oral lysine acetylsalicylate and metoclopramide in the acute treatment of migraine: a multicentre double-blind placebo-controlled study" *Cephalalgia* (1994) 14:297-300.Chabriot "Combined Aspirin and Metoclopramide in the Acute Treatment of Migraine Attacks: A Review" *Headache Quarterly* (1997) 8:118-121.Chrubasik "Paracetamol and metoclopramide in fixed combination" *Med Montasschr Pharm* (1996) 19(4):110 (German language).Cohen "Migraine Headache and the Managed Care Formulary" *Drugs Benefit Trends* (1996) 8(8) 28-30, 33-34,41.Consumers Assoc. "Metoclopramide/analgesic combinations for migraine" *Drug and Therapeutics Bulletin* (1980) 18, No. 24: 95-96.

(List continued on next page.)

Primary Examiner—Jose G. Dees*Assistant Examiner*—Frank Choi(74) *Attorney, Agent, or Firm*—Michael A. Sanzo; Fitch, Even, Tabin & Flannery(57) **ABSTRACT**

The invention is directed to pharmaceutical compositions useful in the treatment of migraine. The compositions contain metoclopramide and one or more NSAIDs in unit dosage form. By selecting NSAIDs that are non-acidic or segregating the metoclopramide and NSAID, the storage life of the compositions has been increased. Also disclosed are coordinated dosage forms for the sequential release of drugs. The invention encompasses methods of treating migraine using any of these dosage forms.

41 Claims, 5 Drawing Sheets